UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

DATE: 18 DECEMBER 2007

SUBJECT: FIPRONIL – Occupational Exposure/Risk Assessment for the Proposed Use of Fipronil to Control Fire Ants in Field Grown Ornamentals

PC Code: 129121 DP Code: 346777

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INTRODUCTION

Under provisions in Section 24(c) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), as amended, the State of Tennessee has requested a Special Local Need registration to use the insecticide fipronil for controlling fire ants in field grown nursery stock.

This memorandum serves as the ARIA/RD's assessment of exposure and risk to occupational pesticide handlers (mixers, loaders, applicators) and agricultural workers. It should be noted that the risk assessment techniques used in this document are those that have been developed and refined by the Health Effects Division (HED)/Office of Pesticide Programs' Science Policy Council for Exposure (ExpoSAC). Therefore, the risk assessment methods are the same as those used by HED and are HED standard operating procedure (SOP).

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USE PATTERN SUMMARY

The product requested for use is TOPchoice™ insecticide. The use pattern summary is taken from the TOPchoice™ Insecticide label (EPA Reg. No. 432-1217) and from the Tennessee 24(c) submission (supplemental label). TOPchoice™ is a granular formulation which contains 0.0143 % active ingredient (ai) fipronil.

The label directs applicators, mixers, loaders and persons cleaning application equipment to wear long sleeved shirt, long pants, waterproof gloves and shoes plus socks as personal protective equipment (PPE).

There is a 24 hour restricted entry interval (REI).

The rate of application for the proposed 24(c) use is 175 lb formulation/A (0.025 lb ai/A). It may applied in "split" (*i.e.* 2) applications of 75 lb formulation/A. Split applications are separated by a two week reapplication interval.

According to the 24(c) label, applications should be broadcast applications "in and around areas where in-ground ornamental trees are grown in commercial nurseries...For best results, the treated area should be irrigated after application."

The label directs that it may NOT be used on bare ground, or areas where plants may be grown for food. It may NOT be applied to pastures or grazing lands.

See Table 1.0 for a summary of the proposed use pattern.

Table 1.0 Summary of Proposed Use Pattern for Fipronil Applied to Commercial Nurseries to Control Imported Fire Ants

Formulation	TOPchoice™ Insecticide; 0.0143 % ai granular; Reg. No. 432-1217
Method of Applic.	Push-type cyclone spreader, tractor mounted granular spreader
Applic. Rate	175 lb formulation/A (0.025 lb ai/A) (*maximum single app.*) 87 lb formulation/A (0.0124 lb ai/A)
Max. No. Applications	1/yr at the high rate 2/yr at the low rate
Applic. Interval	14 days
Preharvest Interval	4 – 24 weeks prior to harvest of in-ground ornamental trees
Restricted Entry Interval	24 hours
Manufacturer	Bayer Environmental Science

OCCUPATIONAL PESTICIDE HANDLER EXPOSURE

Based upon the proposed use pattern, ARIA/RD believes the most highly exposed occupational pesticide handlers would be 1) mixer/loader using open pour loading of granules, 2) an applicator using open-cab, tractor mounted, broad cast; and 3) a mixer/loader/applicator using a push-type "cyclone" spreader.

In this situation, RD believes applications are most likely made by private growers versus commercial applicators. As such, exposures are expected to be short-term duration exposures. Treatment blocks are expected to be rather small as compared to many field crops. Entire nurseries will not be treated at one time. The crops that are to be "harvested" need to be certified as free of fire ants.

Particularly for ground applications, private (*i.e.,* grower) applicators may perform all functions, that is, mix, load and apply the material. The HED ExpoSAC SOP Number 12 (29 March 2000) directs that although the same individual may perform all those tasks, they shall be assessed separately. The available exposure data for combined mixer/loader/applicator scenarios are limited in comparison to the monitoring of these two activities separately. These exposure scenarios are outlined in the Pesticide Handler Exposure Database (PHED) Surrogate Exposure Guide (August 1998). HED has adopted a methodology to present the exposure and risk estimates separately for the job functions in some scenarios and to present them as combined in other cases. Most exposure scenarios for hand-held equipment (such as hand wands, backpack sprayers, and push-type granular spreaders) are assessed as a combined job function. With these types of hand held operations, all handling activities are assumed to be conducted by the same individual. The available monitoring data support this and HED presents them in this way. Conversely, for equipment types such as fixed-wing aircraft, groundboom tractors, or air-blast sprayers, the applicator exposures are assessed and presented separately from those of the mixers and loaders. By separating the job functions, HED determines the most appropriate levels of PPE for each aspect of the job without requiring an applicator to wear unnecessary PPE that might be required for a mixer/loader (*e.g.,* chemical resistant gloves may only be necessary during the pouring of a liquid formulation).

No chemical specific data were available with which to assess potential exposure to pesticide handlers. The estimates of exposure to pesticide handlers are based upon surrogate study data available in the PHED (v. 1.1, 1998). For pesticide handlers, it is HED standard practice to present estimates of dermal exposure for "baseline" that is, for workers wearing a single layer of work clothing consisting of a long sleeved shirt, long pants, shoes plus socks and no protective gloves as well as for "baseline" **and the use of protective gloves** or other PPE as might be necessary.

The Agency's most recent consideration of the fipronil toxicological database was presented in November 2005 (B. Hanson, DP Codes, 3318905, Memo 19 JUNE 2007, "Petition Number: 5F6948 – AMENDED Human Health Risk Assessment for Fipronil Incorporating the IR-4 Section 3 Petition for Registration on Onion and Shallot Seed (dry bulb) and a Proposed Permanenet Tolerance on Tuberous and Corm Vegetables and

(Crop Group 1C)"). In the Agency's review, a short-term duration (1 - 30 days) dermal toxicological endpoint was identified from a 21-day dermal toxicity study in the rabbit. The No Observable Adverse Effects Level (NOAEL) is 5.0 mg ai/kg bw/day and the toxic effects noted were decreased body weight gain and food consumption in both sexes. A 70 kg body weight is used to calculate dermal exposure. Since the dermal toxicological endpoint was identified from a dermal study, there is no adjustment for dermal absorption.

A short-term duration inhalation endpoint was identified from a developmental neurotoxicity study in the rat. The NOAEL is 0.05 mg ai/kg bw/day and the toxic effects seen were decreases in group mean pup weights during lactation and significant increase in time of preputial separation in males. Since the inhalation toxic effects were identified from a developmental study with fetal effects, a 60 kg bw is used to calculate inhalation exposure. HED and RD assume 100% absorption via the inhalation route of exposure. See Table 1.0 for a summary of estimated exposures and risks and see the ATTACHMENT for a summary of toxicological endpoints used for risk assessment.

Table 2.0 Summary of Exposure & Risk for Occupational Handlers Applying Fipronil to Nursery Stock

Unit Exposure[1] mg ai/lb handled		Applic. Rate[2] lb ai/unit	Units Treated[3]	Avg. Daily Exposure[4] mg ai/kg bw/day		MOE[5]	COMBINED MOE[6]
Mixer/Loader Open Pour Loading Granules							
Dermal:				Dermal:			
SLNoGlove	0.0084	0.025	80 A/day	SLNoGlove	0.00024	20,833	841
SLWithGlove	0.0069	lb ai/A		SLWithGlove	0.00019	26,315	848
Inhal.	0.0017			Inhal.	0.000057	877	
Applicator Open cab Granule Broadcast							
Dermal:				Dermal:			
SLNoGlove	0.0099	0.025	80 A/day	SLNoGlove	0.00028	17,857	1168
SLWithGlove	0.0072	lb ai/A		SLWithGlove	0.00021	23,809	1187
Inhal.	0.0012			Inhal.	0.00004	1,250	
Mixer/Loader/Applicator Push-type Cyclone Spreader							
Dermal:				Dermal:			
SLNoGlove	2.9	0.025	5 A/day	SLNoGlove	0.0052	961	769
SLWithGlove	no data	lb ai/A		SLWithGlove	no data		
Inhal.	0.0063			Inhal.	0.000013	3,846	

1. Unit Exposures are taken from "PHED SURROGATE EXPOSURE GUIDE", Estimates of Worker Exposure from The Pesticide Handler Exposure Database Version 1.1, August 1998. Inhal. = Inhalation. Units = mg a.i./pound of active ingredient handled.
2. Applic. Rate. = Taken from the proposed 24(c) label
3. Units Treated ExpoSAC SOP 9.1 Revised 25 SEPT 2001
4. Average Daily Dose (ADD) = Unit Exposure * Applic. Rate * Units Treated ÷ Body Weight (60 kg for inhalation and 70 kg for dermal).
5. MOE = Margin of Exposure = No Observable Adverse Effect Level (NOAEL) ÷ ADD. NOAEL = No Observable Adverse Effect Level (5.0 mg a.i./kg bw/day for short-term dermal and 0.05 mg ai/kg bw/day for inhalation)
6 Combined MOE = $\frac{1}{\frac{1}{MOE_{Dermal}} + \frac{1}{MOE_{Inhalation}}}$

A MOE of 100 is adequate to protect occupational pesticide handlers from exposures to fipronil resulting from the proposed use pattern. Since the combined MOEs are greater than 100, these exposures do not exceed ARIA/RDs level of concern.

POSTAPPLICATION EXPOSURE TO AGRICULTURAL WORKERS

Post application exposure is expected to be negligible for the proposed use pattern. 1) The product is applied to the soil (ground). 2) The label lists a preharvest interval of 4 – 24 weeks. 3) Harvesting of field grown ornamentals is largely accomplished by mechanical means. 4) The label suggests irrigation after application for best results. Therefore, ARIA/RD believes postapplication exposures would not equal or exceed those estimated for occupational pesticide handlers. Therefore, the proposed use does not exceed ARIA/RDs level of concern.

RESTRICTED ENTRY INTERVAL (REI)

No REI is stated on the proposed supplemental label. The REI listed on the TOPCHOICE label is 24 hours.

Since fipronil is classified in Acute Toxicity Category II for inhalation and dermal (based on the rabbit study), the worker protection standard (WPS) interim REI is 24 hours. The REI stated on the TOPCHOICE label is adequate to protect agricultural workers from postapplication exposures.

Acute Toxicity Data on *FIPRONIL*

Guideline No./ Study Type	MRID No.	Results	Toxicity Category
870.1100 Acute oral toxicity -rat	42918628	LD50 = _ 92/_ 103 mg/kg; _+_ 97 mg/kg	II
870.1200 Acute dermal toxicity	42918629 42918630	LD50 = > 2000 mg/kg [rat] = 354 mg/kg [rabbit]	III II
870.1300 Acute inhalation toxicity -rat	43544401	LC50 = _ 0.36/_ 0.42 mg/L; _+_ 0.39 mg/L	II
870.2400 Acute eye irritation -rabbit	42918632	mild transient ocular irritant	III
870.2500 Acute dermal irritation - rabbit	42918633	slight dermal irritant	IV
870.2600 Skin sensitization -Guinea Pig	42918634	non-sensitizing	

ATTACHMENT

Summary of Toxicological Dose and Endpoints for Fipronil for Use in Human Risk Assessment[1].

Exposure Scenario (Fipronil)	Dose Used in Risk Assessment, UF	FQPA SF and Endpoint for Risk Assessment	Study and Toxicological Effects
Acute Dietary all populations including infants and children	NOAEL= 2.5 mg/kg UF = 100 **Acute RfD** = 0.025 mg/kg	FQPA SF = 1 **aPAD** = acute RfD / FQPA SF = 0.025 mg/kg	Acute neurotoxicity - rat LOAEL = 7.0 mg/kg based on: decreased hindleg splay in males at 7 hours.
Chronic Dietary all populations	NOAEL= 0.019 mg/kg/day UF = 100 **Chronic RfD** = 0.0002 mg/kg/day	FQPA SF = 1 **cPAD** = chr RfD / FQPA SF = 0.0002 mg/kg/d	Chronic/carcinogenicity study - rat LOAEL = 0.059 mg/kg/day based on: increased incidence of seizures and death, alterations in clinical chemistry (protein), increased TSH, and decreased T4.
Short-Term Oral (1-7 days) (Residential)	oral study LOAEL ≤0.1 mg/kg/day UF of 3 for no NOAEL, 100 for interspecies extrapolation and intraspecies variation	**LOC for MOE** = 300 (Residential, includes the FQPA SF)	Developmental toxicity Study - rabbit LOAEL = ≤ 0.1 mg/kg/day based on: maternal toxicity of decreased body weight gain, decreased food consumption, and decreased food efficiency.
Intermediate-Term Oral (1 week - several months) (Residential)	oral study LOAEL ≤0.1 mg/kg/day UF of 3 for no NOAEL, 100 for interspecies extrapolation and intraspecies variation	**LOC for MOE** = 300 (Residential, includes the FQPA SF)	Developmental Toxicity Study - rabbit LOAEL = ≤ 0.1 mg/kg/day based on: maternal toxicity of decreased body weight gain, decreased food consumption, and decreased food efficiency.
Short-Term Dermal (1-7 days) (Occupational/ Residential)	dermal study NOAEL= 5 mg/kg/day	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100 (Residential, includes FQPA SF)	21-Day dermal toxicity study - rabbit LOAEL = 10.0 mg/kg/day based on: decreased body weight gain, and food consumption in both sexes.
Intermediate-Term Dermal (1 week - several months)	dermal study NOAEL= 5 mg/kg/day	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100	21-Day dermal toxicity study - rabbit LOAEL = 10.0 mg/kg/day based on: decreased body weight gain, and food consumption in both sexes.

(Occupational/ Residential)		(Residential, includes FQPA SF)	
Long-Term Dermal (several months - lifetime) (Occupational/ Residential)	oral study NOAEL= 0.019 mg/kg/day (dermal absorption rate = 1%)	**acceptable MOE** = 100 (Occupational) **acceptable MOE** = 100 (Residential, includes FQPA SF)	Chronic/carcinogenicity study - rat LOAEL = 0.059 mg/kg/day based on: increased incidence of seizures and death, alterations in clinical chemistry (protein), increased TSH, and decreased T4.
Short-Term Inhalation (1-7 days) (Occupational/ Residential)	oral study NOAEL= 0.05 mg/kg/day (inhalation absorption rate = 100%)	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100 (Residential, includes FQPA SF)	Developmental neurotoxicity - rat LOAEL = 0.90 mg/kg/day based on: decrease in group mean pup weights during lactation, and significant increase in time of preputial separation in males (dietary).
Intermediate-Term Inhalation (1 week - several months) (Occupational/ Residential)	oral study NOAEL= 0.05 mg/kg/day (inhalation absorption rate = 100%)	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100 (Residential, includes FQPA SF)	Developmental neurotoxicity - rat LOAEL = 0.90 mg/kg/day based on: decrease in group mean pup weights during lactation, and significant increase in time of preputial separation in males (dietary).
Long-Term Inhalation (several months - lifetime) (Occupational/ Residential)	oral study NOAEL= 0.019 mg/kg/day (inhalation absorption rate = 100%)	**acceptable MOE** = 100 (Occupational) **acceptable MOE** = 100 (Residential, includes FQPA SF)	Chronic/carcinogenicity rat study LOAEL = 0.059 mg/kg/day based on: increased incidence of seizures and death, alterations in clinical chemistry (protein), increased TSH, and decreased T4.
Cancer (oral, dermal, inhalation)	Group C - possible human carcinogen	Use chronic RfD to estimate human risk	Increases in thyroid follicular cell tumors with fipronil (male/female)

[1] UF = uncertainty factor, FQPA SF = FQPA Safety Factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic) RfD = reference dose, LOC = level of concern, MOE = margin of exposure.

NOTE: The ATTACHMENT is taken from: (B. Hanson, DP Codes, 316795, 322527, 322529, Memo 15 NOV 2005, "Petition Number: 05OR18 - **Human Health Risk Assessment for Fipronil** - Incorporating the Section 18 Proposal for the Use of Fipronil on Turnips and Rutabagas in Oregon and the Renewal Request for use of Fipronil on Corn.").

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